Myhre syndrome

Myhre syndrome is a condition with features affecting many systems and functions of the body.

People with Myhre syndrome usually have delayed development of language and motor skills such as crawling and walking. Most have intellectual disability that ranges from mild to moderate. Some have behavioral issues such as features of autism or related developmental disorders affecting communication and social interaction.

People with Myhre syndrome often have hearing loss, which can be caused by changes in the inner ear (sensorineural deafness), changes in the middle ear (conductive hearing loss), or both (mixed hearing loss).

Growth is reduced in people with this disorder, beginning before birth and continuing through adolescence. Affected individuals have a low birth weight and are generally shorter than about 97 percent of their peers throughout life.

People with Myhre syndrome typically have stiffness of the skin and are usually described as having a muscular appearance. Skeletal abnormalities associated with this disorder include thickening of the skull bones, flattened bones of the spine (platyspondyly), broad ribs, underdevelopment of the winglike structures of the pelvis (hypoplastic iliac wings), and unusually short fingers and toes (brachydactyly). Affected individuals often have joint problems (arthropathy), including stiffness and limited mobility.

Typical facial features in people with Myhre syndrome include narrow openings of the eyelids (short palpebral fissures), a shortened distance between the nose and upper lip (a short philtrum), a sunken appearance of the middle of the face (midface hypoplasia), a small mouth with a thin upper lip, and a protruding jaw (prognathism). Some affected individuals also have an opening in the roof of the mouth (a cleft palate), a split in the lip (a cleft lip), or both.

Other features that occur in some people with this disorder include constriction of the throat (laryngotracheal stenosis), high blood pressure (hypertension), heart or eye abnormalities, and in males, undescended testes (cryptorchidism).

A disorder sometimes called laryngotracheal stenosis, arthropathy, prognathism, and short stature (LAPS) syndrome is now generally considered to be the same condition as Myhre syndrome because it has similar symptoms and the same genetic cause.

Frequency

Myhre syndrome is a rare disorder. Only about 30 cases have been documented in the medical literature. For reasons that are unknown, most affected individuals have been males.

Genetic Changes

Mutations in the *SMAD4* gene cause Myhre syndrome. The *SMAD4* gene provides instructions for making a protein involved in transmitting chemical signals from the cell surface to the nucleus. This signaling pathway, called the transforming growth factor beta (TGF-β) pathway, allows the environment outside the cell to affect how the cell produces other proteins. As part of this pathway, the SMAD4 protein interacts with other proteins to control the activity of particular genes. These genes influence many areas of development.

Some researchers believe that the *SMAD4* gene mutations that cause Myhre syndrome impair the ability of the SMAD4 protein to attach (bind) properly with the other proteins involved in the signaling pathway. Other studies have suggested that these mutations result in an abnormally stable SMAD4 protein that remains active in the cell longer. Changes in SMAD4 binding or availability may result in abnormal signaling in many cell types, which affects development of several body systems and leads to the signs and symptoms of Myhre syndrome.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Other Names for This Condition

- facial dysmorphism-intellectual deficit-short stature-hearing loss
- LAPS syndrome
- laryngotracheal stenosis, arthropathy, prognathism, and short stature

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Myhre syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0796081/

Other Diagnosis and Management Resources

- Centers for Disease Control and Prevention: Types of Hearing Loss
  https://www.cdc.gov/NCBDDD/hearingloss/types.html
- National Institute on Deafness and Other Communication Disorders: Communication Considerations for Parents of Deaf and Hard-of-Hearing Children
  https://www.nidcd.nih.gov/health/communication-considerations-parents-deaf-and-hard-hearing-children

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Short Stature
  https://medlineplus.gov/ency/article/003271.htm
- Health Topic: Developmental Disabilities
  https://medlineplus.gov/developmentaldisabilities.html
- Health Topic: Hearing Disorders and Deafness
  https://medlineplus.gov/hearingdisordersanddeafness.html

Genetic and Rare Diseases Information Center

- Myhre syndrome
  https://rarediseases.info.nih.gov/diseases/2572/myhre-syndrome

Additional NIH Resources

- Eunice Kennedy Shriver National Institute of Child Health and Human Development: Intellectual and Developmental Disabilities
  https://www.nichd.nih.gov/health/topics/idds/Pages/default.aspx
- National Institute on Deafness and Other Communication Disorders: Communication Considerations for Parents of Deaf and Hard-of-Hearing Children
  https://www.nidcd.nih.gov/health/communication-considerations-parents-deaf-and-hard-hearing-children

Educational Resources

- Centers for Disease Control and Prevention: Intellectual Disability Fact Sheet
  https://www.cdc.gov/ncbddd/actearly/pdf/parents_pdfs/IntellectualDisability.pdf
- Centers for Disease Control and Prevention: Types of Hearing Loss
  https://www.cdc.gov/NCBDDD/hearingloss/types.html
- Disease InfoSearch: Myhre syndrome
  http://www.diseaseinfosearch.org/Myhre+syndrome/9782
- MalaCards: myhre syndrome
  http://www.malacards.org/card/myhre_syndrome
- Orphanet: Myhre syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=2588
- Washington University in St. Louis Neuromuscular Disease Center
  http://neuromuscular.wustl.edu/mother/mlarge.html#myhre

Patient Support and Advocacy Resources

- Little People of America
  http://www.lpaonline.org/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/myhre-syndrome/
- The Arc: for People with Intellectual and Developmental Disabilities
  http://www.thearc.org/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28myhre+syndrome%5BTIAB%5D%29+OR+%28laps+syndrome%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D

OMIM

- MYHRE SYNDROME
  http://omim.org/entry/139210

Sources for This Summary

- Burglen L, Héron D, Moerman A, Dieux-Coeslier A, Bourguignon JP, Bachy A, Carel JC, Cormier-Daire V, Manouvrier S, Verloes A. Myhre syndrome: new reports, review, and differential diagnosis. J Med Genet. 2003 Jul;40(7):546-51. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12843331
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1735530/
- Caputo V, Cianetti L, Niceta M, Carta C, Ciolfi A, Bocchinfuso G, Carrani E, Dentici ML, Biamino E, Belligni E, Garavelli L, Boccone L, Melis D, Andria G, Gelb BD, Stella L, Silengo M, Dallapiccola B, Tartaglia M. A restricted spectrum of mutations in the SMAD4 tumor-suppressor gene underlies Myhre syndrome. Am J Hum Genet. 2012 Jan 13;90(1):161-9. doi: 10.1016/j.ajhg.2011.12.011.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22243968
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3257749/
- Le Goff C, Mahaut C, Abhyankar A, Le Goff W, Serre V, Afenjar A, Destrée A, di Rocco M, Héron D, Jacquemont S, Marlin S, Simon M, Tolmie J, Verloes A, Casanova JL, Munnich A, Cormier-Daire V. Mutations at a single codon in Mad homology 2 domain of SMAD4 cause Myhre syndrome. Nat Genet. 2011 Dec 11;44(1):85-8. doi: 10.1038/ng.1016.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22158539
- Lindor NM, Gunawardena SR, Thibodeau SN. Mutations of SMAD4 account for both LAPS and Myhre syndromes. Am J Med Genet A. 2012 Jun;158A(6):1520-1. doi: 10.1002/ajmg.a.35374. Epub 2012 May 14.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22585601
- Lindor NM. LAPS syndrome and Myhre syndrome: two disorders or one? Am J Med Genet A. 2009 Feb 15;149A(4):798-9. doi: 10.1002/ajmg.a.32719.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19267408
- McGowan R, Gulati R, McHenry P, Cooke A, Butler S, Keng WT, Murday V, Whiteford M, Dikkers FG, Sikkema-Raddatz B, van Essen T, Tolmie J. Clinical features and respiratory complications in Myhre syndrome. Eur J Med Genet. 2011 Nov-Dec;54(6):e553-9. doi: 10.1016/j.ejmg.2011.07.001. Epub 2011 Jul 21.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21816239

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